PATENT SPECIFICATION

NO DRAWINGS.

Inventors: - DON PIERRE RENE LUCIEN GIUDICELLI and CHARLES HENRI GENOT



Date of Application and filing Complete Specification: No. 16874/61. May 9, 1961.

Complete Specification Published: Aug. 22, 1962.

Index at Acceptance:—Class 81(1), B2(C:H:S), B2(C:H:S). International Classification: -A61k.

COMPLETE SPECIFICATION.

Therapeutic Preparations Containing 7-Substituted Theophylline Derivatives.

We, LES LABORATOIRES DAUSSE, a French Body Corporate, of 4 rue Aubriot, Paris, France, do hereby declare the invention, for which we pray that a patent may be granted 5 to us, and the method by which it is to be performed, to be particularly described in and by the following statement:-

This invention relates to therapeutic preparations containing 7-substituted theo-

phylline derivatives.

According to the present invention there is provided a therapeutic composition of matter comprising (a) a purine component having a musculotropic action which is a water-soluble, 15 7-substituted theophylline derivative, such as $7 - \beta$ - hydroxy - ethyl theophylline, $7 - \beta - \gamma$ - dihydroxypropyl theophylline and salts of theophylline - 7 - ethanoic acid; and (b) an adrenergic component which is the hydrochloride of 1 - (3:4 - dihydroxyphenyl)-2-methylamino-1-propanol.

It has been found that a medicinal synergy exists between the hydrochloride of 1-(3:4dihydroxyphenyl) - 2 - methylamino - 1 - propanol and the purine components as herein-

before defined.

The potentiated bronchodilatory effect-obtained by the administration of the composition - containing 1 - (3:4 - dihydroxy, phenyl) - 2 - methylamino - 1 - propanol, acting by means of an adrenergic mechanism, and the above-defined purine components, of which the action is mainly musculotropic, are particularly useful in the treatment of bronchial dyspnea and more especially asthma.

This potentiation has been shown by the method of recording the tonus of the bronchi of the guinea pig as described by Halpern

(Arch. Int. Pharmacodyn. et Therap., 1942,

The minimum active doses A and P of the adrenergic component and of the purine component on acetylcholinic bronchospasm having been determined, doses A1 and P1 of each of these components, lower than the doses A and P respectively, are chosen, and it is found that they have no action on the bronchospasm produced by the injection of acetylcholine.

Continuing the experiment, there are simultaneously administered to the guinea pig the dose A1 of adrenergic component and the dose P1 of purine component, and it is found that this association is capable of 55 inhibiting and sometimes even suppressing the bronchospasm produced by acetylcholine, the latter being employed in the same dose throughout the experiment.

Thus, the simultaneous administration of an ineffective does A1 of the hydrochloride of 1 - (3:4 - dihydroxyphenyl) - 2 - methylamino-1-propanol and of an ineffective dose P1 of a purine component, or of a mixture of purine components, produces by mutual potentiation an unexpected bronchodilatory effect, since it is greater than the sum of the effects peculiar to each of the constituents of the composition.

The new synergic compositions have many advantages.

In the first place they permit of obtaining a considerable bronchodilatory effect by utilising only small quantities of the substances constituting the composition. Thus, the desired therapeutic effect can be fully obtained despite the reduction of the posology of each of the constituents, which results in a

	· · · · · · · · · · · · · · · · · · ·	• • • • • • • • • • • • • • • • • • • •
	lowering of the toxicity without a diminution	(2) 1 - (3:4 - Dihydroxyphe-
	of the activity.	nyl) - 2 - methylamino - 1-
	For example, it is known that adrenergic	propanol hydrochloride 0.025 g.
5	substances, of which 1-(3:4-dihydroxphenyl)- 2 - methylamino - 1 - propanol hydrochloride	7 - β - γ - Dihydroxypropyl
-	is one, produce fairly frequently tachycardia	theophylline 4 g. 70
	and signs of central excitation which result in	Reducing solvent q.s 50 ml.
	trembling of the extremities, notably of the	
	hands, and insomnia.	In both cases, the reducing solvent em-
0	The synergic action of the purine bases	ployed is a solution of the following com-
	makes it possible to reduce the dose of 1.	position :—
	(3:4 - dihydroxyphenyl) - 2 - methylamino-	
	1-propanol and to reduce to a very consider-	Sodium bisulphite solution 2.5 ml. 75
=	able extent, or to eliminate, the secondary	Disodium sulphite 0.50 g.
5	effects in question.	
	Since the purine bases also have central	Distilled water q.s 1000 ml.
	stimulating effects characterised essentially by insomnia, it is desirable to add to the	Tell and the state of the state
	synergic compositions of the present inven-	It is to be noted that these solutions can be
)	tion a quantity of a drug which is a barbituric	distributed in 1 ml. or 2 ml. ampoules, so
	derivative. Butobarbital or butylethyl-	that there are obtained either ampoules con- 80
	malonylurea has proved particularly desir-	taining ½ mg. or ampoules containing 1 mg. of 1 - (3:4 - dihydroxyphenyl) - 2 - methyl-
	able from this standpoint.	amino-1-propanol hydrochloride.
	The compositions may comprise in addi-	These ampoules (preferably those of 1 ml.
	tion one or more other purine substances	containing only ½ mg. of 1-(3:4-dihydroxy- 85
	selected from the ophylline, the ophylline ethy-	phenyl) - 2 - methylamino - 1 - propanol hy-
	lenediamine and caffeine.	drochloride) may be used for shallow sub-
	The new compositions are of value in the	cutaneous or intramuscular injections.
	treatment of respiratory troubles of bronchial or pulmonary origin, of asthma, of pulmonary	•
	emphysema, of chronic bronchitis, of pul-	T) TT
	monary sclerosis, of chronic catarrh of the	EXAMPLE II.
	respiratory passages and of silicosis.	Aqueous solution for atomisation:— 90
	The purine component and the adrenergic	(1) Ampoule A
	component may be associated with an	1 - (3:4 - Dihydroxyphe-
	excipient for suppositories, an aqueous	nyl) - 2 - methylamino - 1-
	excipient for parenteral administration, an	propanol hydrochloride 0.01 g.
	aqueous excipient for administration by the	Monosodium sulphite solu- 95
	aerial route or an excipient for oral admini- stration.	tion 0.003 ml.
	When the composition is used in an aqueous	Distilled water q.s 1 ml.
	medium, it is desirable to take account of the	
	tendency of the diphenol, which is 1-(3: 4-di-	_
	hydroxyphenyl) - 2 - methylamino - 1 - pro-	Ampoule B
	panol, to oxidise in the presence of com-	7 - β - γ - Dihydroxypropyl
	pounds having an alkaline reaction. It is	theophylline 0.375 g. 100
	therefore important to avoid the choice of a	Distilled water q.s 10 ml.
	theophylline derivative having an alkaline	. To am
	reaction and it is preferred that there should	The section of the
	be included in the aqueous medium an anti-	The contents of the two ampoules are
	oxidant or a reducing agent which is acceptable from the representation	mixed and the mixture administered in
	able from the pharmacological viewpoint,	aerosol form by discharge from a pressurised container.
	for example sodium bisulphite or sodium formaldehyde sulphoxylate.	
	Examples of pharmaceutical forms of the	(2) The following single solution compositions may also be adopted, the reducing sol-
	compositions of the present invention are the	vent being that which is specified for solutions
	following:—	intended for parenteral administration.
	Example I.	T
	Parenteral Administration :-	1 /9 / Athendrometer to 5
	(1) 1 - (3:4 - Dihydroxyphe-	1 - (3 : 4 - dihydroxyphenyl) - 2-
	nyl) - 2 - methylamino 1-	methylamino - 1 - propanol
	propanol hydrochloride 0.025 g.	hydrochloride 0.01 g.
	7 - β - γ - Dihydroxypropyl	7 - β - γ - Dihydroxypropyl theo-
	the ophylline \dots 2.50 g.	phylline 0.30 g.
	Reducing solvent q.s 50 ml.	Reducing solvent q.s 10 ml. 115

Example III. Suppositories:— (i) For adults:— (ii) For adults:— (iii) For adults:— (iv) For adults:— (iv) Part Alebas — (iv) Part Alebas — (iv) Part Part Part Part Part Part Part Part			•		
Suppositories:— (i) For adults:—		EXAMPLE III.		Lac varnish 0.005 g.	
10 For adults:— 1				Absorbent powder 0.005 g.	
1 · (3 : 4 · Dihydroxypopy) theophylline				Taleum 0.02 g.	55
1		1 - (3:4 - Dihydroxyphe-		Crystallised sugar . 0.13 g.	
propanol hydrochloride	5	nyl) - 2 - methylamino - 1-		Erythrosin traces	
Tablets 1. (3 : 4 - Dihydroxyphonyl theophylline 1. (3 : 4		propanol hydrochloride	0.005 g.	Carnauba wax traces	
theophylline 0.30 g. Solium hydrosulphite 0.002 g		7 - β - γ - Dihydroxypropyl		•	
Example IV. Tablets: O.002 g. Caffeine . 0.004 g. Caffeine . 0.002 g. Maize starch . 0.012 g. Potato starch . 0.012 g. Parafin oil 0.002 g. Parafin oil . 0.002 g.				WHAT WE CLAIM IS:—	
Entectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.)		Sodium hydrosulphite	0.002 g.		eΩ
regetable origin (m.p. + 35° C.)	10	Eutectic mixture of glycer-		I. A therapeutic composition of matter	Ю.
Soluble 7.substituted theophylline derivative; and (b) an adrenergic component which is the hydrochloride of 1.(3 : 4-dihydroxyphenyl) - 2 - methylamino - 1 - propanol hydrochloride		ides of fatty acids of natural		comprising (a) a purine component naving a	
tive; and (b) an adrenergic component which is the hydrochloride of 1-(3:4-dihydroxyphenyl) - 2 - methylamino - 1 - propanol hydrochloride		vegetable origin (m.p. +		musculotropic action which is a water-	
(2) For infants:— 1 · (3 : 4 · Dihydroxyphenyl) - 2 · methylamino · 1 · propanol hydrochloride · · · · · · · · · · · · · · · · · · ·		35° C.)	1.655 g.	soluble 7-substituted theophyline deriva-	
1 1 · (3 : 4 - Dihydroxyphenyl) - 2 - methylamino - 1 - propanol hydrochloride 7 · β · γ · Dihydroxypropyl theophylline Sodium hydrosulphite Cochineal carmine Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) 30 With butobarbital 1 · (3 : 4 - Dihydroxyphennyl) - 2 - methylamino - 1 - propanol hydrochloride 7 · β · γ · Dihydroxyphennyl) - 2 - methylamino - 1 - propanol hydroxyphenyl theophylline Sodium hydroxyphennyl Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) Example IV. Tablets : 40 7 · β · γ · Dihydroxypropyl theophylline 1 · (3 : 4 · Dihydroxypropyl theophylline Example IV. Tablets : 40 7 · β · γ · Dihydroxypropyl theophylline 1 · (3 : 4 · Dihydroxypropyl theophylline 2 · A composition according to Claim 1 or 2 wherein the purine component and the adrenergic component are associated with an aqueous excipient for suppositories, an aqueous excipient for parenteral administration, an aqueous excipient for oral administration. 30 G. Θ.			•	tive; and (b) an adrenergic component	65
nyl) - 2 - methylamino - 1 - propanol hydrochloride		(2) For infants:—		which is the hydrochioride of 1-(3.4-un-	w
Propanol hydrochloride 7 - β - γ - Dihydroxypropyl theophylline	15				
T - β - γ - Dihydroxypropyl theophylline 0.0019 g.		nyi) - 2 - methylamino - 1-	0.0015.5	2 A composition according to Claim 1	
theophylline Sodium hydrosulphite Cochineal carmine Cochineal carmine Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 1 · (3 : 4 - Dihydroxypnenyl) + 2 · methylamino - 1 · propanol hydrochloride Sodium hydrosulphite		propanol hydrochloride	0.0019 g.	wherein the theonhylline derivative is 7.8-	
Sodium hydrosulphite			0.085 %	hydroxyethyl theophylline 7-8-y-dihydroxy-	70
Cochineal carmine Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.)	96			propel theophylline or a salt of theophylline-	
Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35°C.) 1.800 g. (3) With butobarbital:— 1 · (3 : 4 · Dihydroxyphenyl) · 2 · methylamino · 1 · propanol hydrochloride 0.005 g. Butobarbital 0.05 g. Sodium hydrosulphite 0.005 g. Example IV. Tablets:— 40 7 · β · γ · Dihydroxyproyl theophylline 0.06 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.06 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.002 g. Sodium hydrosulphite 0.005 g. Example IV. Tablets:— 40 7 · β · γ · Dihydroxyproyl theophylline 0.06 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.06 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 : 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 · Dihydroxyproyl) theophylline 0.006 g. 1 · (3 · 4 ·	20				
ides of fatty acids of natural vegetable origin (m.p. + 35° C.) 1.800 g. (3) With butobarbital:—			0.00016.		
vegetable origin (m.p. + 35° C.) 1.800 g.		ides of fatty acids of natural		2 wherein the purine component and the	
25 35° C.) 1.800 g. (3) With butobarbital :— 1 · (3 : 4 · Dihydroxyphenyl) · 2 · methylamino · 1 · propanol hydrochloride		veretable origin (m.p. +		adrenergic component are associated with an	75
(3) With butobarbital:— 1 · (3 : 4 - Dihydroxyphenyl) - 2 · methylamino - 1- propanol hydrochloride 30	25		1.800 g.	excipient for suppositories, an aqueous	
(3) With butobarbital:— 1 · (3 : 4 · Dihydroxyphenyl) - 2 · methylamino - 1- propanol hydrochloride 0.005 g. 30 7 · β · γ · Dihydroxypropyl theophylline 0.05 g. Sodium hydrosulphite 0.05 g. Sodium hydrosulphite 0.005 g. Sodium hydrosulphite 0.002 g. Example IV. Tablets:— Tablets:— 40 7 · β · γ · Dihydroxypropyl theophylline 0.004 g. Caffeine 0.004 g. Caffeine 0.006 g. 1 · (3 : 4 · Dihydroxypropyl theophylline 0.006 g.) I · (3 : 4 · Dihydroxypropylline 0.006 g.) I · (4 · Composition according to claim 5 of Claim 5 of Claim		00 01,	Ü	excipient for parenteral administration, an	
1 - (3 : 4 - Dihydroxyphenyl) - 2 - methylamino - 1 - propanol hydrochloride 0.005 g. 30		(3) With butobarbital:—		aqueous excipient for administration by the	
ryl) - 2 - methylamino - 1 - propanol hydrochloride 0.005 g. 7 - β - γ - Dihydroxypropyl theophylline 0.05 g. Sodium hydrosulphite 0.05 g. Sodium hydrosulphite 0.002 g. Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) 1.605 g. Example IV. Tablets :— 10 7 - β - γ - Dihydroxypropyl theophylline 0.04 g. Caffeine 0.06 g. 1 - (3:4 - Dihydroxypropyl theophylline 0.06 g. 1 - (3:4 - Dihydroxypropyl theophylline 0.06 g. 1 - (3:4 - Dihydroxypropyl theophylline 0.002 g. Maize starch 0.012 g. Maize starch 0.0125 g. Paraffin oil 0.002 g. 0.005 g. 0.002 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.003 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.002 g. 0.002 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.002 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.003 g. 0.002 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g. 0.003 g		1 - (3:4 - Dihydroxyphe-		aerial route or an excipient for oral admini-	90
T - β - γ - Dihydroxypropyl theophylline 0.30 g. Sodium hydrosulphite 0.005 g. Sodium hydrosulphite 0.002 g. Sodium hydrosulphite 0.004 g. Sodium hydrosulphite 0.002 g. Sodium hydrosulphite 0.004 g. Sodium h		nyl) - 2 - methylamino - 1-		stration.	00
theophylline Butobarbital Sodium hydrosulphite Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) Tablets: 10 7 - β - γ - Dihydroxy-propyl theophylline ine Popyl theophylline ine 10 3 : 4 - Dihydroxy-phenyl - 2 - methylamino - 1 - propanol hydrochloride Icing sugar 0.02 g. Maize starch . 0.01 g. Paraffin oil 0.002 g. Maize starch . 0.01 g. Paraffin oil 0.002 g. Butobarbital 0.05 g. 0.05 g. 0.002 g. 5. A composition according to any of Claims 1—4 which contains in addition a drug which is a barbituric acid derivative. 6. A composition according to Claim 5 which contains butobarbital. 7. A composition according to any of Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, London W C1		propanol hydrochloride	0.005 g.	4. A composition according to Claim 5	
Sodium hydrosulphite 0.05 g. 0.002 g. 5. A composition according to any of Claims 1—4 which contains in addition a drug which is a barbituric acid derivative. 6. A composition according to Claim 5 which contains butobarbital. 7. A composition according to Claim 5 which contains butobarbital. 7. A composition according to any of Claims 1—6 which further contains one or more other purine substances selected from theophylline thylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. 8. A KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn., London W C1	30	7 - β - γ - Dihydroxypropyl	0.90 ~	wherein the excipioni contains a pharma-	
Sodium hydrosulphite 0.002 g. Eutectic mixture of glycerides of fatty acids of natural vegetable origin (m.p. + 35° C.) 1.605 g. EXAMPLE IV. Tablets:— 1.605 g. EXAMPLE IV. Tablets:— 40 7 - β - γ - Dihydroxy-propyl theophylline 0.04 g. Caffeine 0.06 g. 1 - (3:4 - Dihydroxy-phenyl - 2 - methylamino - 1 - propanol hydrochloride 0.01 g. Icing sugar 0.02 g. Maize starch 0.01 g. Potato starch 0.0125 g. Potato starch 0.002 g. Paraffin oil 0.002 g. Sodium hydrosulphite 0.002 g. Claims 1—4 which contains in addition a drug which is a barbituric acid derivative. 6. A composition according to Claim 5 which contains butobarbital. 7. A composition according to any of Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as hereinbefore described with reference to any of the foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, London W C1		theophylline	~ ~~		•
Eutectic mixture of glycer- ides of fatty acids of natural vegetable origin (m.p. + 35° C.)				5 A composition according to any of	85
ides of fatty acids of natural vegetable origin (m.p. + 35° C.)		Somm nydrosupine	0.002 g.	Claims 1—4 which contains in addition a	
vegetable origin (m.p. + 35°C.)	25	ides of fatty soids of natural		drug which is a barbituric acid derivative.	
Tablets:— Tablets:— 1.605 g. which contains butobarbital. 7. A composition according to any of 90 Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 1.605 g. which contains butobarbital. 7. A composition according to any of 90 Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples. 1.605 g. which contains butobarbital. 7. A composition according to any of 90 Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples. 1.605 g. A composition according to any of 90 Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples. 1.605 g. A composition according to Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples. 1.605 g. A composition according to Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic Composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples.	อบ			6. A composition according to Claim 5	
Tablets:— 40 7 - β - γ - Dihydroxy- propyl theophyl- line 0.04 g. Caffeine 0.06 g. 1 - (3 : 4 - Dihydroxy- phenyl - 2 - methyl- amino - 1 - propa- nol hydrochloride 1 0.02 g. Maize starch 0.01 g. Portato starch 0.01 g. Paraffin oil 0.002 g. Paraffin oil 0.002 g. Paraffin oil 0.002 g. Tablets:— 7. A composition according to any of go Claims 1—6 which further contains one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein-before described with reference to any of the foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, Lendon W. C.1			1.605 g.	which contains butobarbital.	
Tablets:— 40 7 - β - γ - Dihydroxy- propyl theophyl- line 0.04 g. Caffeine 0.06 g. 1 - (3 : 4 - Dihydroxy- phenyl - 2 - methyl- amino - 1 - propa- nol hydrochloride ling sugar 0.02 g. Maize starch 0.01 g. Portato starch 0.01 g. Paraffin oil 0.002 g. Paraffin oil 0.002 g. Claims 1—6 which further contants one or more other purine substances selected from theophylline, theophylline ethylenediamine and caffeine. 8. A therapeutic composition of matter according to Claim 1 substantially as herein- before described with reference to any of the foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, Lendon W.C.1		<i>50 C.)</i>	0	7. A composition according to any of	90
theophylline, theophylline ethylenediamine and caffeine. 1 · (3 : 4 · Dihydroxy-phenyl - 2 · methylamine - 1 · propanol hydrochloride Icing sugar · · · · · · · · · · · · · · · · · · ·		Example IV.		Claims 1—6 which further contains one or	
 7 - β - γ - Dihydroxy-propyl theophylline 0.04 g. Caffeine 0.06 g. 1 - (3 : 4 - Dihydroxy-phenyl - 2 - methylamino - 1 - propanol hydrochloride Icing sugar 0.02 g. Maize starch 0.01 g. Potato starch 0.0125 g. Paraffin oil 0.002 g. Paraffin oil		Tablets:—		more other purine substances selected from	
propyl theophyline 0.04 g. Caffeine 0.06 g. 1 - (3 : 4 - Dihydroxy-45 phenyl - 2 - methylamino - 1 - propanol hydrochloride Icing sugar 0.02 g. Maize starch 0.01 g. Potato starch 0.01 g. Paraffin oil 0.002 g. 0.002	40	7 - β - γ - Dihydroxy-			
Caffeine 0.04 g. Caffeine 0.06 g. 1 - (3 : 4 - Dihydroxy- phenyl - 2 - methyl- amino - 1 - propanol hydrochloride Icing sugar 0.02 g. Maize starch 0.01 g. Paraffin oil 0.002 g. Paraffin oil 0.002 g. Lendon W.C.1		propyl theophyl-		and caffeine.	95
1 - (3 : 4 - Dihydroxy- phenyl - 2 - methyl- amino - 1 - propa- nol hydrochloride Icing sugar 0.02 g. Maize starch 0.01 g. Potato starch 0.0125 g. Paraffin oil 0.002 g. I - (3 : 4 - Dihydroxy- before described with reference to any of the foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, Lendon W C1				8. A therapeutic composition of matter	00
phenyl - 2 - methyl- amino - 1 - propa- nol hydrochloride 0.01 g. Icing sugar 0.02 g. Maize starch 0.01 g. Potato starch 0.0125 g. Paraffin oil 0.002 g. Isomorphic foregoing specific examples. J. A. KEMP & CO., Chartered Patent Agents, 14 South Square, Gray's Inn, Lendon W.C.1				according to Claim I substantially as herem-	
amino - 1 - propanol hydrochloride 0.01 g. Nucleus : J. A. KEMP & CO., Icing sugar 0.02 g. 0.20 g. Chartered Patent Agents, Maize starch 0.01 g. 14 South Square, Faraffin oil 0.002 g. Gray's Inn, Icing sugar 0.02 G. Gray's Inn, Icing sugar 0.02 G. Chartered Patent Agents, Iding sugar				before described with reference wany of the	
nol hydrochloride 0.01 g. Nucleus: J. A. KEMP & Co., Icing sugar 0.02 g. Chartered Patent Agents, Maize starch 0.01 g. Potato starch 0.0125 g. Paraffin oil 0.002 g. Gray's Inn, I and on W.C.1	45			foregoing specific examples.	
Icing sugar 0.02 g. O.20 g. Chartered Patent Agents, Maize starch . 0.01 g. Potato starch . 0.0125 g. Paraffin oil 0.002 g. Gray's Inn, Lendon W.C.1		amino - I - propa-	Muslama :	T A KTEMP & CO.	
Maize starch 0.01 g. 14 South Square, 50 Potato starch 0.0125 g. Gray's Inn, Paraffin oil 0.002 g. Lendon W.C.1					
50 Potato starch 0.0125 g. Gray's Inn, Paraffin oil 0.002 g. London W.C.1			v.20 g.		
Paraffin oil 0.002 g. London W.C.1				-	
	90			Gray's Inn,	
Taioum 0.0100 B.)				London, W.C.1.	

Abingdon: Printed for Her Majesty's Stationery Office, by Burgess & Son (Abingdon), Ltd.—1962.
Published at The Patent Office, 25, Southampton Buildings, London, W.C.2,
from which copies may be obtained.